LETTERS

Diabetic Ketoacidosis in Children

The case report on ketoalkalosis in Rett syndrome by Cameron *et al*., contains some interesting biochemistry.[1] The pO_2 on admission was said to be 36.5 kilopascals. Room air at STP has a partial pressure of oxygen around 20 kilopascals, so I presume this patient was breathing oxygen. If so, how much and why?

The serum osmolality was measured at 334, while calculation suggests that it should have been at least 360. What caused that discrepancy?

I am puzzled also as to why half strength saline was used for rehydration. This patient was not seriously hyperosmolar and half strength saline has been associated with the development of cerebral oedema.

Finally, why should an X-linked disorder affect only females?

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Reference

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Diabetic Ketoacidosis in Children: Authors' Reply

We are glad of the opportunity to reply to Dr Daggett's comments. The first blood gas with high PaO_2 was taken shortly after admission to the ward, at a time when the child would have been breathing supplemental oxygen following transportation. A large osmolar gap may occur in certain cases of poisoning, administration of mannitol, and inherited metabolic disorders. We have made an error in using the blood sugar value of 46.1 mmol l^{-1} (it should have been 18.6 mmol l^{-1}). At the time of initial laboratory osmolar measurement of 334 mosmol kg^{-1} the calculated osmolality was 318 mosmol kg^{-1}, which is an abnormally raised osmolar gap (see below). An X-linked disorder can affect only females if it is associated with embryolethality in males which is thought to be true of Rett syndrome.

The issue of fluid administration and the development of cerebral oedema in children with diabetic ketoacidosis remains controversial. Articles and editorials have remarked that efforts to relate fatal brain herniation to specific aspects of treatment have been fruitless,[1] suggesting to some that it is merely a marker of severity rather than the treatment administered. Several theories have been put forward as to why cerebral oedema develops as a complication of diabetic ketoacidosis[2] which include: haemoconcentration; stasis and local cerebral anoxia; abnormal capillary permeability allowing sodium ions to diffuse freely into cells; rapid reduction in blood glucose concentration following insulin therapy, resulting in disparity with cerebrospinal fluid glucose concentration, which then results in a marked osmotic shift of water across the blood brain barrier; accumulation of 'polyols', creating an osmotic gradient in the white matter; and, paradoxical lowering of cerebrospinal fluid pH in relation to blood pH related to bicarbonate administration, which may lead directly to local cerebral hypoxia. A concern in the clinical literature has been the possibility that some aspect of fluid administration or glucose therapy may contribute to the development of cerebral oedema. It should however be remembered that in severe cases of diabetic ketoacidosis cerebral oedema may well be a universal feature, which may even be present before treatment is initiated.[3–6] In a review of 17 case reports Rosenbloom *et al*.[7] identified no specific factor as being associated with the development of the cerebral oedema. This review did not substantiate that overrapid rehydration or correction of blood glucose was a feature common to all cases. In contrast, Duck and Wyatt[3] have argued that rapid fluid therapy (>4 l m^{-2} day^{-1}), together with the development of hyponatraemia or fall in calculated sodium at the time of falling glucose is a significant factor in the production of cerebral oedema. More recently in 1990, in a retrospective review of 119 patients, Harris *et al*.[8,9] observed that complications attributable to cerebral oedema were more likely to occur among patients with failure of their concentration of sodium to rise as glucose declined. In view of this, these authors then studied prospectively 58 episodes of diabetic ketoacidosis in 40 patients aged between 18 months and 20 years. By using a 48 h treatment plan to provide fluid replacement for dehydration (with half the deficit in sodium being given in the first 12 h of treatment), they found that the serum sodium concentration rose as glucose declined in 55 (95 %) of the 58 episodes. Importantly no patient developed a major complication. Their two main conclusions were: (1) failure of the serum sodium concentration to rise as glucose concentration declined is a marker of excessive administration of free water; (2) an expanded rehydration period, with repair fluid containing an average of 125 mmol l^{-1} of sodium early in therapy, will usually protect against a rapid decline in effective serum osmolality.

While there is no absolute standard for fluid resuscitation and treatment in children with diabetic ketoacidosis, there are certain principles that the majority of physicians would accept.[10] These include an initial rapid correction of hypovolaemia with isotonic fluid such as normal saline (containing 150 mmol l^{-1} of sodium), which is then followed by a phase of replacing the estimated fluid deficit over the next 24 to 28 h. Generally half of the calculated deficit is replaced over the first 8 to 12 h of treatment. In addition urinary losses and insensible requirement (approximately 40 % of usual maintenance) are given. After the first 8 h of therapy hyperglycaemia should be mild or resolved, and ongoing urinary losses need not be replaced. After the initial resuscitation phase, the type of fluid used for intravenous therapy is tailored to the patient's serum electrolytes. Insulin is usually started within 1–2 h of treatment. Finally, as stated by Krane,[10] 'prudence would indicate that if hypotonic fluids are used for rehydration of the child with diabetic ketoacidosis, serum sodium should be followed closely, and the amount of sodium in the intravenous fluid increased if the serum sodium declines'.

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 CCC 0742–3071/98/040348–02$17.50

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Myocardial Infarction on a 17-year-old Diabetic Adolescent

Four to six per cent of all deaths under the age of 40 years occur in patients with diabetes mellitus.[1] Although this figure may appear small, the circumstances of such deaths are not always clear. A 17-year-old boy, found dead, with evidence of acute myocardial infarction is reported. We gratefully acknowledge the parents' permission for doing this.

The patient was born on 9 November 1978. He was the second child, born to healthy parents. Our patient's history was unremarkable until December 1985 when he developed Type 1 diabetes mellitus. Following a brief 'honeymoon' period he was treated with two daily injections of insulin, until 1993, when he was changed to three premeal injections of soluble insulin (human Actrapid Penfill) and one of Ultratard (20 units) before bedtime. His recent dosage was Actrapid 12 units before breakfast, 10 units before lunch, and 8 units before supper. He was on a 2500 kcal nutritional regimen (divided approximately into 500, 1000, and 1000 kcal for breakfast, lunch and supper) and exercised moderately.

He was last seen in our Centre on 18 January 1996. He was 17 years old and had had Type 1 diabetes for 10 years. His height was 176 cm, he weighed 59 kg, and BP was 110/70 mmHg. Physical examination was unremarkable. Laboratory work-up included HbA_{1C} 6.8 %, microalbuminuria of 18.2 μg min^{-1}, GFR 138 ml min^{-1}, renin 1.25 ng l^{-1}, T4 91.4 nmol l^{-1}, TSH 4.4, serum creatinine 77.5 μmol l^{-1}, serum cholesterol 5.3 mmol l^{-1}, triglycerides 63 mg dl^{-1}, HDL-C 2 mmol l^{-1}, LDL-C 2.97 mmol l^{-1}, Apo A1 194, B 69.8, Lp(a) $<$ 10.3.

On 15 March 1996 he went to bed with a blood glucose of 8.9 mmol l^{-1} 4 hours following the last injection of fast acting insulin and supper. He had not exercised on that day, consumed about 75 g rice as an evening snack, and did not receive any other medication. He did not seem to be restless during sleep. Nonetheless, he was found dead in bed at 7 am. The autopsy showed congested lungs. The heart weighed 320 g. The coronary vessels were slightly atheromatous. An ischaemic region was noticed in the rear myocardial wall and the left ventricle, with a recent haemorrhagic infiltration. The myocardium was brittle and soft. No other organ lesions were reported. The medical examiner's report attributed the death to a recent acute myocardial infarction.

Interest in unexpected and unexplained deaths in young patients with diabetes mellitus was raised following a report by Tattersall and Gill[2] of the so-called 'dead-in-bed syndrome'. They reported 22 deaths on apparently good health diabetic patients. The cause of death was not established. Four similar deaths occurred in Bergen, Norway, during the years 1988–1990.[3] On the basis of these observations a nationwide retrospective investigation was conducted by the same authors.[1] Autopsies performed on 13 of their cases did not reveal any cause of death. Twelve patients, however, were reported as having had frequent episodes of hypoglycaemia. The authors postulated that introduction of human insulin and multiple daily injections may be implicated in hypoglycaemic attacks, when right control is applied.

Although, hypoglycaemia could be considered in our patient, this seems unlikely, as he had not exercised that day, his blood glucose was slightly elevated (8.9 mmol l^{-1}), he had his supper, and the action of the fast acting insulin should have been fading. Moreover, the autopsy findings were confirmatory of acute myocardial infarction.

It is our belief that diabetologists of children and adolescents should be prepared to face unexplained deaths. Whether young patients with Type 1 diabetes should have a periodic cardiovascular evaluation remains debatable. There is evidence, however, of early cardiovascular lesions in childhood Type 1 diabetes, shown by others and recently by our group.[4,5]

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